Investigating Magainin through Computational Molecular Modeling

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Introduction

Proteins are essential to life, and a lot of the work they do within the body involves binding and interacting with cell membranes. Because of this, understanding exactly how these proteins interact with the membranes is important. Magainin is an antimicrobial peptide found in the skin of the *Xenopus laevis,* also known as the African Clawed Frog[2]. It is comprised of 23 amino acids and has a helical structure. Magainin is important because it can disrupt electrochemical gradients in the cell membranes of many bacteria, tumors and fungi[1], which is extremely useful for pharmaceuticals.

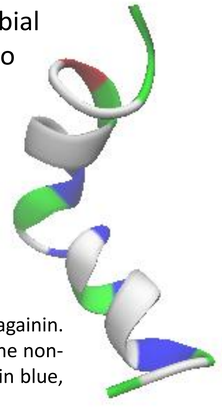

Figure 1. VMD image of Magainin.
Each color on the protein represents a different property of Magainin. Magainin's structure allows it to have many different properties. The non-polar regions of Magainin are depicted in white, the basic regions in blue, acidic regions in red, and polar regions green.

Experimental

Multiple software programs are used to create and analyze the bilayer system, including the Chemistry at Harvard Macromolecular Mechanics Guided User Interface (CHARMM-GUI), Nanoscale Molecular Dynamics (NAMD), Visual Molecular Dynamics (VMD), and the Highly Mobile Membrane-Mimetic Model (HMMM)[3]. These programs were used to build the simulation system and then export and view/analyze it at the end. To look at how Magainin bound to the membranes, two different conditions were created, one where a model skin cell membrane contained protonated lignoceric acid, and the other non-protonated lignoceric acid. Both conditions used the HMMM model to shorten the lipid tails in the membrane. Five simulations were created for each of these conditions and they were each run for about 300 nanoseconds on Deepthought2, the University of Maryland's supercomputer. Once the simulation finished running, the output files were opened in VMD to analyze the binding patterns of Magainin.

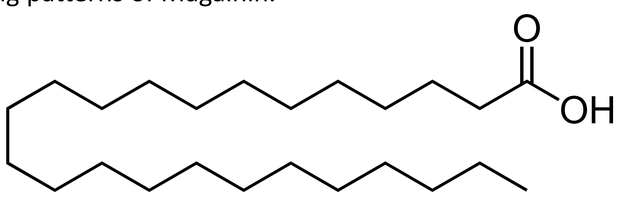

Figure 2. Structure of protonated lignoceric acid. Deprotonated lignoceric acid has a negative charge, and it missing the hydrogen on the end of the carboxylic acid group.

Results

Membrane Protein System

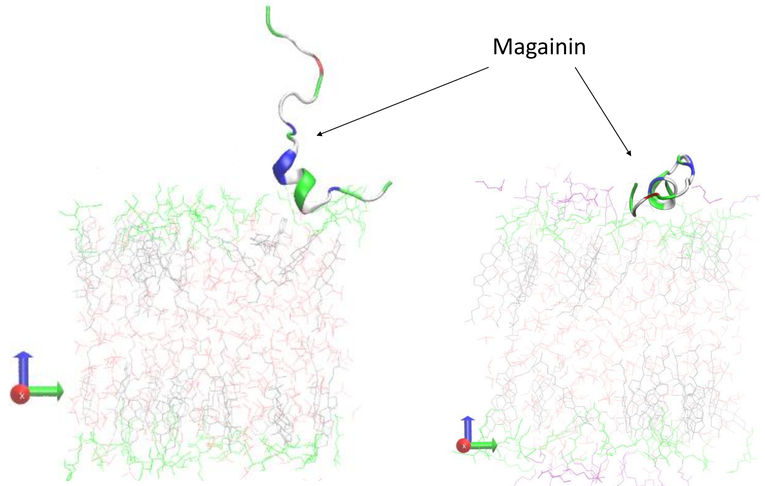

Figure 3. The bound state of Magainin at 150 nanoseconds for a deprotonated membrane simulation.

Figure 4. The bound state of Magainin at 150 nanoseconds for a protonated membrane simulation.

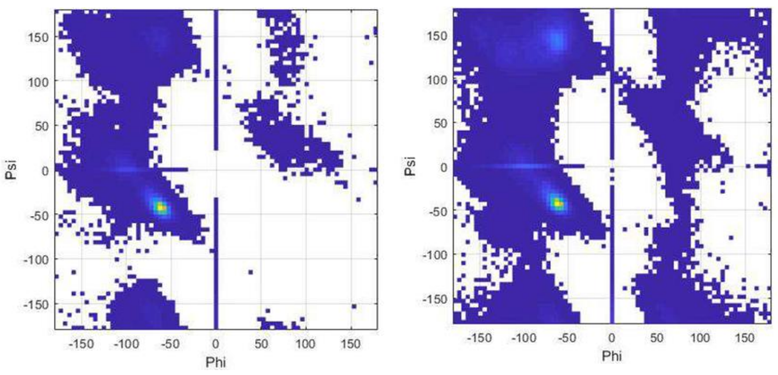

Figure 5. Ramachandran plot of the system in Figure 3 at the beginning of the simulation (left) and after 300 nanoseconds (right).

LIGN1		
	Start	End
Alpha helix (%)	72.64	43.07
Beta sheet (%)	15.45	40.71
Alpha beta border (%)	0.67	0.74
Turn (%)	0.78	1.82
Rest (%)	10.47	13.67

Figure 6. A table describing the secondary structure of Magainin at the start and end of the simulation. Data is taken from the Ramachandran plots shown in Figure 5.

Conclusion

Magainin's behavior varies greatly when placed near a model skin cell membrane. The bound states of Magainin are different for protonated and deprotonated systems. Additionally, the secondary structure of Magainin is altered greatly during its interactions with a model skin cell membrane. The peptide loses nearly 50% of its helical structure, one of its distinct properties. Magainin is an extremely interesting peptide, and our simulations will hopefully continue to probe its unique properties.

Future Work

To further analyze the binding states of Magainin, the simulations are being converted to full atom simulations (instead of the short HMMM model) and being run for 300 nanoseconds as full atom simulations. The full atom simulations will allow for deeper analysis and a better look at the bound states of Magainin, and hopefully will provide insight into why Magainin behaves so differently in changing environments.

Acknowledgements

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References

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